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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,964	11/28/2000	Tessa Crompton	CIBT-P01-080	7789

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EXAMINER

BRANNOCK, MICHAEL T

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/724,964

Applicant(s)

CROMPTON, TESSA

Examiner

Michael Brannock

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,3,6-31 and 33-55 is/are pending in the application.
- 4a) Of the above claim(s) 3,19,20,22-28 and 30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,6-18,21,29,31 and 33-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth in Paper 20, 4/8/03, have been entered in full.

Claims 3, 19, 20, 22-28 and 30 have been withdrawn previously.

Applicant is reminded that the instant claims are being examined only to the extent that they read on the elected invention, i.e., the administration of a benzene modified sonic hedgehog polypeptide for the inhibition of an immune response, as set forth previously.

Maintained Rejections:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 6-18, 21, 29, 31, and new claims 33-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of suppressing or promoting thymic T-cell maturation comprising administering a polypeptide at least 100% identical to the N-terminal auto-proteolytic fragment of a hedgehog polypeptide, wherein said peptide binds a naturally occurring patched protein, does not reasonably provide enablement for the broad scope of suppressing or enhancing the immune function or immune system of an animal, nor for modulating T-cell maturation other than in the thymus (e.g. peripheral T-cell maturation), nor for any form of therapy, and nor for the suppression or promotion of T-cell

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maturation comprising the administration of a hedgehog agonist thereof other than a polypeptide at least 100% identical to the N-terminal auto-proteolytic fragment of a hedgehog polypeptide or antagonistic antibody that binds there to. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims. The rejection is maintained for the reasons of record.

Applicant relies on the reasons of record which have been fully considered previously and not found persuasive. Additionally, Applicant cites Reidhaar-Olson et al. as evidence that techniques of combinatorial chemistry have now trivialized the search for important residues in a protein. This argument has been fully considered but not deemed persuasive. One of ordinary skill in the art appreciates that this research paper speaks nothing about the ability of an artisan to find functional variants of the hedgehog protein. This can be found on page 56, col 2, second full paragraph wherein the authors discuss the necessary features of their technique. In item (ii), the authors assert that they use a “functional selection to identify genes encoding active proteins”. This functional selection is an assay wherein bacteria that contain the active variants of this particular bacterial virus gene are selected for. There is no such selection technique available for hedgehog proteins known in the art and nor has the instant specification provided any. Further, the Authors used only a small fragment known to provide all of the features required for binding; they only speculate that this technique could “in principle” provide data for the entire protein (see the last paragraph of page 56). These facts do not support Applicant’s assertion that such techniques have “trivialized the once complex and painstaking process of making and testing polypeptide variants”. To the contrary, this paper further demonstrates that we are as yet a long way away from being able to make and test variants trivially. There simply

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does not exist an assay wherein the activation of patched could be monitored as taught by

Reidhaar-Olson et al.

Applicant argues that Bowie teaches that, in a given protein, perhaps 50% of single amino acid changes could be expected to yield an normal or nearly normal protein. And given this, applicant asserts that even random substitution would be expected give rise to a majority of variants with normal activity. This argument has been fully considered but not deemed persuasive. First, Applicant's claims are not limited to single amino acid substitutions. A protein that is 90% identical to the N-terminal autoproteolytic fragment of sonic hedgehog would have 17 substitutions relative to wild-type. If it is true that each substitution had a 50% chance of rendering a non-functional protein, then the chance of making a functional protein would be that same as that of flipping a coin and having it land on heads 17 times in a row! Second, the skilled artisan would not consider the random testing and choosing of single functional mutants and then mixing and matching them to practice the invention commensurate in scope with the claims to be routine experimentation, even if that could be done in a straight-forward manner, i.e. even if the affects of each mutation were simply additive.

Applicant urges the artisan would know to only make conservative substitutions. This argument has been fully considered but not deemed persuasive. As taught by Bowie et al, it is simply unpredictable what the effect of amino acid substitution will be, even "conservative" substitutions, see p.1306, column 2, paragraph 2, of Bowie.

On page 11 of the response, Applicant argues, essentially, that because several different wild-type hedgehog proteins have been shown to work in various functional assays, then one would expect that artificially constructed variants should be expected to work as well. This

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argument has been fully considered but not deemed persuasive. Presumably, applicant is pointing to the large range of natural variation as evidence that these proteins are tolerant to change. Regarding the concept of natural vs. artificial; the variation between the naturally occurring forms has been guided by hundreds of millions of years of evolutionary pressure, wherein mutations arise randomly, and those that work are kept. The instant specification has provided nothing more than this essentially random trial and error strategy of evolution to try to make such variants.

Applicant argues that the claims are allowed to encompass inoperative embodiments. This argument has been fully considered but not deemed persuasive. The issue is that the specification has failed to teach how to make operative embodiments without undue experimentation.

Claims 2, 6-9, 11-18, 21, 29, 31, and new claims 33-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record.

Applicant argues that the claims have been amended to obviate the rejection. This argument has been fully considered but not deemed persuasive. Only claim 10 has been amended to obviate the rejection. The remaining claims require a tremendous genus of hedgehog agonist proteins that are not described in the specification, as set forth for the reasons of record.

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Conclusion

No claims are allowable.

This application contains claims drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (571) 272-0871.


Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB



February 8, 2004



YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600